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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/716,841	11/17/2000	Roger Briesewitz	STAN-130	8223

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EXAMINER
NAFF, DAVID M

ART UNIT	PAPER NUMBER
1651	15

DATE MAILED: 08/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/716,841	Briesewitz et al
Examiner	**Group Art Unit**
K. Ford	1651

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 7/25/03.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 16, 17, 19-32 + 51-66 is/are pending in the application.

Of the above claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 16, 17, 19-32 + 51-66 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 11 filed 2/19/03

☒ Notice of Reference(s) Cited, PTO-892

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Interview Summary, PTO-413

☐ Notice of Informal Patent Application, PTO-152

☐ Other _____

Office Action Summary

In view of new grounds of rejection, the final rejection of 2/25/03 is withdrawn and prosecution on the merits is reopended.

The amendment of 7/25/03 has been entered. The amendment canceled claims 1-15, and amended claims 16, 23, 28, 51, 57 and 62.

Claims examined on the merits are 16, 17, 19-32 and 51-66, which are all claims in the application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 21, 26, 31, 55, 60 and 65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are unclear by not having clear antecedent basis for "said drug target". The claims on which these claims depend do not recite "drug target".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 16, 17, 19-32 and 51-66 are rejected under 35 U.S.C. 102(e) as being anticipated by Briesewitz et al (6,372,712 B1).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The claims are drawn to modulating a pharmacokinetic property such as half-life or hepatic first-pass metabolism of a drug by administering a bifunctional molecule of less than 5000 daltons molecular weight consisting of the drug and a pharmacokinetic modulating moiety which may be jointed to the drug by a linker.

Briesewitz et al disclose administering to a host a bifunctional molecule of less than 5000 daltons molecular weight consisting of a drug moiety and a presenter protein ligand joined to the drug moiety. The drug moiety binds to a drug target and the presenter protein ligand binds to a presenter protein. The drug moiety exhibits at least one of enhanced affinity, specificity or selectivity for the target as compared to a free drug control. For example, see claims 1-15. The ligand may be for peptidyl prolyl isomerase (claim 6).

When administering a bifunctional molecule as disclosed by Briesewitz et al, modulating a pharmacokinetic property as presently claimed will be an inherent result.

Claim Rejections - 35 USC § 103

Claims 16, 17, 19-32 and 51-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nygren et al (WO 91/01743) and Pouletty et al (5,843,440).

The claimed invention is described above.

Nygren et al disclose extending the half-life of a biologically active protein or peptide such as a drug by binding the drug to a polypeptide fragment capable of binding to a serum protein.

Pouletty et al disclose modulating pharmacokinetics with a bifunctional reagent that is a conjugate of a binding member specific for a blood-borne target agent and a binding member specific for a long-lived blood associated entity (col 1, lines 40-49). The conjugate finds therapeutic use by reducing effective concentration of a blood-borne agent having detrimental biological activity in a host. The blood-borne agent may be a growth factor, coagulation factor, enzyme, toxin, drug, microbe, autoreactive immune cell, or infected or tumorous cell. The conjugate has therapeutic use of reducing biological activity or effective concentration of free agent, modulating volume distribution of the agent, targeting the agent to sites of enhanced immune response or facilitating agent clearance from the blood stream (abstract and col 2, lines 23-26). Binding of the conjugate specifically to the target agent

and the long-lived blood associated entity extends the life of the conjugate (col 12, lines 22-26, and claims 1-8).

It would have been obvious to use a small-molecule drug in conjugates as suggested by Nygren et al and Pouletty et al since small molecule drugs are conventionally used for treatments, and the conjugates of Nygren et al and Pouletty et al can contain a drug or a binding member that has the function of a drug. Modulating half-life of a drug and extending lifetime of a conjugate as disclosed by Nygren et al and Pouletty et al would have inherently modulated a pharmacokinetic property and hepatic first-pass metabolism as presently claimed. The use of a linker as in claims 51-66 would have been a matter of obvious choice since linkers are well known for forming conjugates, and Pouletty et al disclose (col 8, lines 25-67) using a wide variety of linkages.

Response to Arguments

Applicant's arguments filed 7/25/03 have been fully considered but they are not persuasive.

Applicants urge that Nygren et al relate to large fusion proteins. However, this is not the case since a fusion protein is an alternative to a protein or peptide covalently linked to a polypeptide fragment. A peptide can have a molecular weight less than 5000 daltons. The polypeptide fragment that binds to serum protein can also be less than 5000 daltons. Therefore, the conjugate of Nygren et al can be less than 5000 daltons, and to use a conjugate of less than 5000 daltons would have been obvious since peptides and fragments are commonly less than 5000 daltons.

Applicants urge that the bifunctional molecule of Pouletty et al does not contain a drug moiety because a free drug is the target. However, the target does not have to be a drug since the target can be host derived or naturally present (col 2, line 23 to col 3, line 9). Therefore, the member that binds to the target can be considered a drug since it reduces harmful effects of a material produced by the host. The modulating moiety of the present claims can be selected to bind to an anchor that is a blood component as disclosed by Pouletty et al. While Pouletty et al may disclose conjugates of large molecules such as two different antibodies as urged by applicants, Pouletty et al also disclose using a fragment of the antibody. Furthermore, Pouletty et al disclose that binding molecules other than antibodies that are specific for the anchor can be used (col 7, lines 46-63). Thus, it is clear that Pouletty et al intend to encompass conjugates of less than 5000 daltons.

Applicants point to claims that require the modulating moiety to bind to intracellular protein. However, Pouletty et al disclose host derived non-cellular target agents (col 2, line 41 to col 3, line 9), some of which are intracellular proteins.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection

based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 16, 17, 19-32 and 51-66 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 6,372,712 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because administering the bifunctional molecule of the patent claims would have inherently modulated a pharmacokinetic property as presently claimed.

Double Patenting

Claims 16, 17, 19-32 and 51-66 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 16-44 and 48-53 of copending Application No. 19/025,936. Although the conflicting claims are not identical, they are not patentably distinct from each other because administering the bifunctional molecule of the claims of the copending application would have inherently modulated a pharmacokinetic property as presently claimed.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone

number is 703-308-0520. The examiner can normally be reached on Monday-Friday about 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 703-308-4743. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is 703-308-0196.

David M. Naff
Primary Examiner
Art Unit 1651

DMN
8/21/03